

The occurrence of a bulbar paralysis makes the prognosis very grave, for, as has been previously stated, death has invariably followed.

**TREATMENT.** Only 4 cases have been operated upon. In 2 cases reported by Kappis the operation had no effect on the eye palsies, although the cardinal and other symptoms of exophthalmic goitre were greatly improved. So far as I am aware the case which I am reporting is the first of the grave ones (with bulbar paralysis) to be operated upon. Kappis reported a third case, one with difficulty in swallowing, which was believed to be due to paralysis of the glossopharyngeus and vagus. The patient died four hours after a lobectomy.

The presence of nerve palsies, excluding possibly the cases with bulbar paralysis, does not contra-indicate surgical intervention. Indeed, it would seem advisable to operate promptly in the hope not only of arresting the progress of the palsy but also of curing the disease.

#### BIBLIOGRAPHY.

Sattler. *Die Basedow'sche Krankheit*, Leipzig, 1909. (Covers literature up to 1909.)

Kappis. *Ueber Gehirnnervenlähmungen bei der Basedow'sche Krankheit*, *Mitt. aus den Grenz. d. Med. u. Chir.*, 1911, xxii, No. 4. (Covers literature between 1909-1911.)

Perdran. *Pigment Occurring in the Dentate Nuclei of the Cerebellum in a Chronic Case of Graves' Disease Associated with Scleroderma and Insanity*. *Jour. Ment. Sci.*, 1914, ix, 497.

Bernhardt. *Basedow'sche Krankheit und Augenmuskellähmung*, *Neur. Centralbl.*, 1911, xxx, 706.

Schlesinger. *Mitt. d. Gesellsch. f. inn. Med. u. Kinderh.*, 1914, xiii, 130.

Krohn. *Chicago Med. Recorder*, 1914, xxxvi, 551.

### THE METABOLISM AND TREATMENT OF RHEUMATOID ARTHRITIS. THIRD PAPER.<sup>1</sup>

BY RALPH PEMBERTON, M.S., M.D.,  
PHYSICIAN TO THE PRESBYTERIAN HOSPITAL, PHILADELPHIA.

(From the Department of Clinical Chemistry in the Pathological Laboratory of the Presbyterian Hospital.)

IN two previous communications<sup>2</sup> the writer has presented a series of cases of rheumatoid arthritis, 18 in all, in which certain laboratory findings and clinical observations were made the basis

<sup>1</sup> Reported before the American Society for the Advancement of Clinical Investigation, Washington, D. C., May 10, 1915.

<sup>2</sup> The Metabolism and Successful Treatment of Chronic Joint Disease; A Preliminary Report, *AMER. JOUR. MED. SCI.*, October, 1912, No. 4, cxliv, 474; and The Metabolism, Prevention, and Successful Treatment of Rheumatoid Arthritis; Second Contribution, *ibid.*, December, 1913, No. 6, cxlvii, 895; January, 1914, No. 1, cxlvii, 111; February, No. 2, p. 265; March, No. 3, p. 423.

of a method of treatment. The results of this were sufficiently encouraging to justify and require a more extended study, with the idea of determining not only the proportion and kinds of cases in which benefit could be expected, but also, if possible, the *modus operandi* of the factors concerned.

The methods in question consist essentially in a curtailment of diet, particularly the carbohydrates and proteins, to a point of tolerance which varies with the individual.

An additional series of cases of rheumatoid arthritis, 19 in number, has accordingly been treated and studied. It is the purpose of this article, therefore, (1) to review the end-results of the first series, where this is possible, some of them dating back five years; (2) to present the results of treatment of the second series of cases, together with some analysis of the failures and successes; (3) to present the results of certain feeding experiments in which the effort was made to determine the specific action, if any, of some foods; and (4) to present the results of laboratory observations, especially upon the hydrogen ion concentration of the urine and the carbon dioxide tension of the alveolar air during the active stages of the disease and during convalescence or recovery therefrom.

**END-RESULTS OF THE FIRST SERIES.** The first series consisted of 18 cases, and a review of them at the present writing brings out several interesting points. No attempt will be made to go into the details of the cases, as these have already been fully given.

Case I was first seen in January, 1911, and remains well, nearly five years afterward.

Cases II, IV, IX, XIII, XVI, and XVII have disappeared from observation.

Cases III and VIII were temperamentally unable, except under close observation, to adhere to any careful régime involving self-denial, and after becoming practically free from active symptoms, deliberately ate what they chose and relapsed.

Cases V and VI are entirely well and leading active lives.

Case VII has run a course of much interest. After making a symptomatic recovery, she slowly lost ground, and in July, 1914, a strict diet modified only slightly an active arthritis. In August she developed acute intestinal obstruction, was operated upon by Dr. John Kennedy, of Philadelphia, and a stenotic band was relieved, after which her arthritis was greatly improved. She felt so well that she ate much more generously, adhering only slightly to the lines of her earlier diet. Her arthritis grew slowly worse, and when last seen, March, 1915, she had definite symptoms, though less than at some previous periods.

The beneficial influence of diet in this case when first treated, the violent exacerbation just preceding acute intestinal obstruction, the relief of symptoms during a long period following the operation, and the gradual increase of the arthritis at first influenced

by a diet and then increasingly less so form a most suggestive sequence of events.

Case X remains well, on duty as a hospital attendant.

Case XI, who was bed-ridden, is free from active arthritis, gets dressed, and walks around one floor of her home. Her chief limitation comes from the ankylosis of her knees in extension, present when first seen. It is of interest to note that there has been present throughout an active leucorrhea which was not properly treated because of the inability to abduct the patient's thighs. This still persists, though the thighs can now be abducted. Her original and subsequently maintained improvement in the face of an obvious source of possible infection is of much interest.

Case XII is reported as active and walking without crutches, and Case XIV is on active duty as a nurse.

Case XV is in buoyant health, and has acquired a considerably increased tolerance for food.

The degree to which patients in this series have differed in their caloric necessities has been noteworthy. Several of them have maintained constant weights upon fewer calories than are generally regarded as practicable in ambulatory cases, as previously noted.

**NEW SERIES.** Space will not permit of giving more than a bare outline of the cases and treatment in this series, together with certain limitations to treatment, except where some particular point necessitates it. In the previous series the full details of each case, together with frequent notes showing the changes of diet and progress, make a repetition of these data in connection with the present cases unnecessary. It should be stated that every case but one was Roentgen-rayed by Dr. W. S. Newcomet, director of the Roentgen-ray department of the Presbyterian hospital, and the clinical diagnosis of arthritis was always thus corroborated. Nearly all of the chronic cases had been through more or less treatment, and some had experienced a great variety.

**CASE XIX.**—Mrs. L., aged sixty-four years, referred by the courtesy of Dr. Walter L. Mendelson, of New York City, was admitted March 28, and discharged June 29, 1914. She presented exophthalmos, enlargement of the thyroid, some tachycardia dating back twenty-five years, an enlarged heart and murmurs. The arthritis was of ten years' duration, affecting the knees, shoulders, and hands. For ten days the patient was watched upon an unrestricted house diet and lost three pounds in weight, averaging 2346 calories per diem, and on April 6 she was given a mixed diet of 1385 calories. By a mixed diet is meant one consisting roughly of one or two eggs, from two to six 30 gm. slices of bread, about 50 gms. of chicken, 15 to 30 gms. of butter, and about 15 gms. of sugar plus green vegetables, according to the desired total. In three days there was some improvement, and on the eleventh day there was no pain in any finger or in the wrist on pressure.

June 17, 1915. Has been doing progressively well for two months. For a month the effort has been made to increase diet, body fat, and weight. Today she feels for the first time some tenderness in the last joint of right ring finger.

The patient left the hospital June 29, with greatly increased bodily activity and hands free except as per last note. Weight, 123 pounds; loss, 16 pounds. She spent the summer at a hotel and followed the diet as well as she could, but grew restive under it. She was seen with Dr. Mendelson in November, 1914. The arthritis of the right ring finger was worse and one other small joint was involved. Her bodily activity, knees, and shoulders were much improved, especially the former two.

Retrospect of this case reveals that the hyperthyroidism was a complicating factor and added to the difficulties of treatment, in that the patient ran an increased pulse-rate throughout and tended easily to lose weight. The long stay in the hospital helped her tremor but made her restive. Her diet was increased too soon, and she admitted that after leaving the hospital she had taken some liberties with it. The entirely favorable application of diet to her arthritis was beyond question, however. The result from her stand-point was an improvement, modified and limited by the complicating hyperthyroidism and by the personal element which led to a curtailment of treatment short of the theoretical ideal.

CASE XX.—Mr. F., aged about fifty-five years, was referred by the courtesy of Dr. Milton J. Lichty, Cleveland, Ohio. Admitted April 9, 1914, discharged July 6, 1914. An arthritis of four and a half years' standing involved practically all joints, and he was confined to a wheel-chair. A probationary house diet showed 3500 to 4000 calories. After several changes the new mixed diet was maintained at 1185 calories. Improvement in the hands began in six days. No changes occurred in the ankylosed joints, but when the patient left the hospital on July 6, 1914, his hands had greatly changed their appearance and he had less pain generally. The loss of weight in three months was twenty-four pounds. This patient was beyond everything but the arrest of the disease in its then stage, but there cannot be any doubt that the causative arthritis was emphatically modified, and in the smaller joints had largely subsided when he left.

CASE XXI.—Mrs. H., aged sixty-three years, was referred by the courtesy of Dr. Hobart A. Hare. She presented an arthritis of four years' duration, involving the knees, shoulders, and hands. She was obese, with myocarditis and loud murmurs. A probationary house diet averaged 2024 calories. She was given a mixed diet of 1271 calories and after six days showed a beginning subsidence of inflammation in the hands. She developed cardiac irregularity and beginning loss of compensation after two weeks of restricted diet, requiring complete rest in bed and stimulation. This diet

was insufficient to accomplish permanent results, and evidently a further reduction was necessary. In view of the heart condition, however, such a step was regarded as dangerous. The patient adhered faithfully to the above diet for three months without any additional improvement in the hope that, though insufficient to arrest the causative arthritis, something might be accomplished. The end-result to her, however, was absolutely *nil*. This case is of value as illustrating the fact that in face of a beginning and distinct response to treatment, as evidenced in the hands, limitations from another source may preclude further efforts. It is important on many counts, as illustrated above, to keep the caloric total as high as possible, from which it follows that in many cases several or more diets have been required before the proper reduction was obtained.

**CASE XXII.**—Mr. P., aged thirty-one years, was referred by the courtesy of Dr. Penn G. Skillern. An arthritis of nine months' duration, immediately following a severe infection of forearm, incapacitated him for work by involvement of hands, knees, and shoulders chiefly. There was no apparent focus of infection anywhere. The patient was a large eater, and began to recover upon a mixed diet of 2500 calories, which were reduced in ten days to about 2000. Progress was steady from the start, and he went home well. Admitted March 3, 1914. Discharged May 2, 1914. Last heard from and well October 15, 1915. The loss of weight in hospital was from 134 to 127 pounds.

**CASE XXIII.**—George W., aged forty-five years, ward case, was admitted June 26, 1913. An arthritis of eight months' duration, involving knees, heels, shoulders, and hands, incapacitated him. His condition was febrile and somewhat suggestive of acute inflammatory rheumatism superimposed on the chronic form. He was given a very low mixed diet of 629 calories for ten days. Undoubted subsidence of the acute symptoms followed. The calories were increased to 1072. The case was not followed beyond July 12, 1913, but the evidence was definitely favorable until then.

**CASE XXIV.**—Mrs. McC., aged fifty-four years, admitted May 25, 1914, discharged August 20, 1914, presented a chronic arthritis of uncertain duration. There were also redness, tenderness, and effusion in knees, ankles, hands, and wrists. Practically every joint was involved, and the symptoms pointed to an acute and severe inflammatory process on top of the chronic form. She was given five glasses of milk in twenty-four hours, increased by eggs chiefly, in course of one week to 1011 calories. Her joints responded from the start, becoming in six days practically painless. Within two days after admission she developed signs of pneumonia, and had a delayed recovery therefrom. The calories were later increased to 1950 to meet the convalescent demands. In January, 1915, her general condition was excellent and the joints were in tolerably

good shape. The social condition of the patient precluded intelligent coöperation.

CASE XXV.—Mrs. R., aged thirty-three years. Was admitted May 22, 1914, discharged July 10, 1914, and had an incapacitating arthritis of three months' duration involving hands, elbows, and knees. Bony deformity of the fingers was present. A probationary house diet averaged 1916 calories. On a mixed diet of 1314 calories she improved at once and steadily. She left the hospital almost free from all symptoms, and has remained entirely well since.

CASE XXVI.—Mrs. S., aged forty-five years, was admitted May 13, 1914, and discharged May 22, 1914. An arthritis of three years' duration involved hands, wrists, elbows, shoulders, knees, and ankles. On a probationary house diet of 1734 calories she began to improve at once and left the hospital against advice when the subjective symptoms had subsided. This case is reported to illustrate the occasional improvement which follows upon the restricted régime of a hospital diet. Comment on this will be made later. Had she stayed a permanent limit of intake would have been assigned her, in the attempt to insure against relapse.

CASE XXVII.—Mrs. C., aged thirty-five years, referred by the courtesy of Dr. A. A. Eshner, was admitted April 27, 1914, and left May 24, 1914. An arthritis of three years' duration involved both hands, wrists, elbows, shoulders, knees, ankles, and feet. A probationary house diet averaged 1933 calories. She improved on 1179 calories of mixed diet, but after ten days became dissatisfied with restrictions and left against advice.

CASE XXVIII.—Mrs. F., aged thirty-nine years, was admitted February 8, 1915, and left February 27, 1915. An arthritis of two years' duration involved spine, jaws, shoulders, elbows, hands, and knees. Four months pregnant. Many fibrous nodules presented along ulnae, tibiae, and around patellæ. She showed some improvement on probationary house diet of 1494 calories, and was given 1396 calories of a fixed diet to insure constancy of intake. Rapid and unmistakable progress followed. She became dissatisfied with restriction of diet, and left against advice. The fibrous nodules had markedly subsided.

CASE XXIX.—Mrs. L., aged about forty-two years, wife of a physician, was referred by the courtesy of Dr. D. J. McCarthy. She was admitted April 19, 1915, and discharged July 5, 1915. An arthritis of nine years' duration involved the shoulders, elbows, wrists, hands, and feet. There were fibroid nodules on both Achilles tendons. A probationary house diet yielded 1850 calories, and she was given a mixed diet of 1191 calories, reduced in two weeks to 1028. Progress was slow but sure. The fibrous nodules and three-quarters of the painful sites were practically gone when she left the hospital. She was instructed to follow her diet all summer

and report in the fall. The loss of weight was from 116 to 105 pounds.

CASE XXX.—Mrs. W., aged about forty-nine years, wife of a physician, was referred by the courtesy of Dr. B. W. Sherwood, of Syracuse, N. Y. Admitted April 20, 1915, discharged June 12, 1915. An arthritis of two and a half years' constant duration, dating back irregularly thirteen years, involved the shoulders, elbows, and hands. This case was of much interest, and was a complete failure. The probationary house diet yielded 2048 calories. New diets were tried of 1294, 1159 and for a short time 674 calories, without clear improvement. An abdominal x-ray was not taken, as customarily on admission, as patient had had this done and the results were reported negative. Upon failure of treatment an x-ray was taken and showed a high degree of visceral stasis, partial collapse of the large bowel, evidence from the bismuth of obstruction in or near the ileum, chronic appendicitis, and possibly duodenal ulcer. The reason for failure cannot be advanced unless it be dependent upon these findings, especially the first two. In discussing the failure with Dr. Sherwood, before the x-rays were taken, the writer cited Case VII (q. r.), as supplying a possible explanation in the obstructive factors there operative. The patient's condition did not suggest, *a priori*, any difficulty of treatment.

CASE XXXI.—Mrs. W., aged about forty years, was referred by the courtesy of Dr. John H. Girvin. A multiple arthritis had for some years involved shoulders, elbows, knees, and hands. Some improvement followed a probationary house diet of 1544 calories. The patient had bad tonsils, and these were removed. It is interesting to note that upon the two days immediately following the operation the patient felt great relief in her joints everywhere, during which time she was nearly without food. As the food was increased the pain and disability returned. The patient then went home to ascertain the end-result of the tonsillectomy, but of her own accord attempted to follow a diet of 1433 calories which she had been given for a few days at the hospital prior to the operation. At this point she disappeared from observation, but was reported later as doing very badly. The points to be noted in this case are the prompt and marked relief coincident with postoperative starvation, ceasing as ingestion of food increased; and the difficulty to be met when patients attempt dietary control by themselves before they are thoroughly accustomed by experience accurately to prepare and follow a diet. Earlier observations on the postoperative relief above recorded helped the writer to formulate the hypothesis upon which this study was started.

CASE XXXII.—Mrs. W., aged about sixty-two years, was referred by the courtesy of Dr. Agnes Vietor, of Boston. Admitted March 9, 1915, discharged June 9, 1915. An arthritis of thirty

years' standing involved nearly every joint in the body except spine and jaws. Myocarditis and mitral regurgitation were present. A probationary house diet yielded 1945 calories. She was placed on a mixed diet of 1080 calories, and improvement began at once, especially in the hands. After one month the case "hung fire." The calories were changed to 1283, of which 753 came from fat. The joints improved further, but her heart-rate increased to 108 and the patient became weak. Her diet was therefore increased eventually to 1700 calories. Her general condition grew stronger, the pulse fell to 85, the pains returned somewhat, especially in knees, but her hands retained their objective and subjective improvement (loss of weight from 161 to 145 pounds). She was instructed to follow this compromise diet all summer. This case showed unquestionable and satisfactory response to diet, but her heart was unequal to carrying her through in the way desired.

CASE XXXIII.—Dr. X., aged thirty-eight years, noticed in early January, 1915, a slight tenderness of the middle joints of some of the fingers of both hands. Toward the end of February there was added to this an ache involving also the lumbar spine. An x-ray, taken and interpreted by Dr. Henry Pancoast, director of the x-ray department of the University of Pennsylvania Hospital, showed inflammatory fog around the affected joints together with rarefaction and overgrowths along the shafts of the bones, an interpretation shared by Dr. Newcomet. Being familiar with some of the writer's cases the patient attempted a diet, and in ten days lost six pounds. He had always been a large eater, particularly of starches and sugars. When seen by the writer he was given a mixed diet of about 1200 calories, and by eight or ten days subjective improvement was established. During an attack of influenza, which then began, he lost more weight, but after about six weeks of adherence to his diet he was entirely free from symptoms, and during August took part in a military encampment, by this time eating much more generously. The diet was carefully carried out in this instance, and the patient himself weighed the ingredients on scales. The loss of weight was about ten pounds in all, from 173 to 163.

FEEDING EXPERIMENTS. The following cases will be detailed at greater length, because they were the subjects of experiments in feeding which developed several points of interest. These experiments were conducted with the full understanding of the patients, who appreciated the possible importance of their co-operative efforts.

CASE XXXIV.—Mrs. S., aged thirty-six years, referred by the courtesy of Dr. Frank Dickson, was admitted November 9, 1914, and discharged February 23, 1915. An arthritis of over seven years' duration, involved the jaws, shoulders, elbows, wrists, ankle, and knees; the hands slightly; the right knee was resected seven years

before. A probationary house diet yielded 1892 calories. On 1072 calories of mixed diet, she improved slowly but steadily, and on January 9, being up and out daily and feeling well, she was given the diet presently to be described.

It should be here stated that for some time the writer had been following the hydrogen ion concentration in the urine of joint cases at various stages of their progress, but no definite conclusions could be reached. The variations of diet in the same and different cases seemed apparently to mask any reaction or fluctuations due to the disease itself, and it was not until the appearance of Blatherwick's "Studies"<sup>3</sup> on the nature of the ash in various foods and its influence upon urinary acidity that these relations became clear and a standard diet could be applied. Accordingly in the following cases one of the diets there described has been utilized as a basis for the study of the urinary acidity of joint cases in health or disease, and also when the influence of certain foods was tested. These standard diets were made up equivalent in caloric value to the mixed diets under consideration, and were chosen without other regard to therapy. The patient was therefore given graham crackers, 75 gms., butter, 36 gms., milk, 720 c.c. per diem = 1009 calories. This was continued for ten days to allow her condition under it to be watched and the urinary acidity to be followed while she was free from symptoms. The basis upon which all the cases in these series have been treated is, in part, that the carbohydrates form at least one of the factors productive of joint disease, and favorable results have followed their curtailment. Other evidence pointed the same way, but the "experimentum crucis" had not been made of inducing the symptoms of the disease by means of pure carbohydrate in a patient previously rendered free from them—a reinduction of the disease, in short.

On the afternoon of January 19, therefore, and twice daily thereafter, the patient was given 62 gms. of "candy" made from cane-sugar, water, a little oil of peppermint to flavor it, and one teaspoonful of vinegar to 528 gms. of sugar. This gave 66 gms. of sugar at each feeding, or 264 calories twice a day, a total ingestion of 528 calories in addition to her regular diet. The total for twenty-four hours was therefore 1089 plus 528, or 1617 calories, an amount somewhat less than the house diet on admission, but considerably greater than that upon which she had improved. It is to be remembered that at this point she was practically free from symptoms, up all day and taking exercise on the porch. The abbreviated notes of her progress follow:

January 22. One joint of left hand shows a slight sensitiveness not present for at least a month.

January 23. Pain increased and present in shoulders and wrist.

<sup>3</sup> The Specific Role of Foods in Relation to the Composition of the Urine, N. R. Blatherwick, Archives Int. Med., September, 1914, xiv, 409-450.

January 24. Hand slightly better. Left shoulder worse. Painful red swelling with effusion just above left elbow. Not sore for six weeks.

January 25. Thumb better but still sore. Elbow and shoulders as before. Jaw on the left painful. Patient is very uncomfortable.

January 26. No candy given today. Jaws worse, both sides equally. Shoulders better. Thumb and knuckles about the same.

January 26. Better as a whole. Jaws, shoulders, and thumb ache less. One joint of left hand has ceased to hurt. Pressure over seventh cervical vertebra elicits soreness and suprascapular muscles on left ache. Undoubted improvement.

January 28. Muscles of back and seventh cervical vertebra are the chief sites of pain. Today patient returns to the mixed diet of 1089 calories, taken before the graham-cracker diet, as the latter has become very monotonous.

January 29. About the same.

January 30 and 31. Better.

February 2. Improvement continues. Muscles of back and neck and the left elbow show some residual soreness. Progress from this date was entirely satisfactory and continued so. Last seen December, 1915, when improvement was maintained. Loss of weight in hospital from 158 to 143 pounds. Comment on this experiment will be made later.

CASE XXXV.—James N., aged forty-four years, referred by the courtesy of Dr. T. T. Thomas, was admitted November 12, 1914, and discharged March 23, 1915. An arthritis of four years' duration, involving shoulders, elbows, wrists, hands, hips, knees, and ankles, incapacitated him. He made noticeable progress on a house diet of 2170 calories, and after a variety of diets of lower caloric value from 1512 to 1829, made steady progress, subject to occasional exacerbations of an acute nature, generally with some effusion. During three months these became less severe and he recovered from them more rapidly, being increasingly free from chronic symptoms in the interim. It was obviously necessary to wait until these exacerbations had become negligible and until observation of the case over a long period of convalescence had shown its true course before a feeding experiment comparable to the last could be attempted. After the patient had been given six or seven different diets, had been watched through six decreasing exacerbations of his chronic arthritis, and was free from pain anywhere in his body, it was thought, on February 16 1915, that a repetition of the carbohydrate feeding would be justified and that any clear response could be ascribed to it. He was accordingly put on 1827 calories, consisting of graham crackers, 100 gms., butter 10 gms., one cup of weak tea with 7 gms. sugar, and one apple of 150 gms. three times a day. For six days he had had practically the same thing, except that 360 of the calories

had been supplied by three glasses of milk per diem; but it was thought advisable to remove, as far as possible, all protein from the diet so that any disturbance referable to the food intake must be due to some other factor in it. Prior to this he had been taking 1512 calories of a mixed diet. A difficulty to be here considered, which had been operative in certain earlier indefinite experiments, was that the patient's total caloric tolerance seemed to be pretty high, as evidenced by the house diet of 2170 calories, on which he showed improvement. This must be exceeded considerably by the sugar calories to have any effect, and such an addition might be physically and psychically difficult of accomplishment. There is a very definite limit to the amount of pure carbohydrate one can willingly take for any length of time. However, beginning with February 16, he was given twice daily 138 and then 150 gms. of candy, made as described in the first case, but without any vinegar. This was equivalent to 150 gms. of cane-sugar, or 600 calories. The patient professed at first to like this and ate it readily, but later did so with great difficulty. The notes of his progress follow.

February 17. Says he feels a little bit stiff in both shoulders, knees, and feet.

February 18. Feels somewhat "tired." Shoulders and knees slightly stiff, but very little so.

February 19. About 7 P.M. yesterday began to feel pain and stiffness in left shoulders, after which pain developed in feet and other joints. Today he has pain on active or passive motion or on pressure at left shoulder, both wrists, between the first and second metacarpophalangeal articulations of left hand, at right thumb (slightly), at second metacarpophalangeal joint of left hand (which hand cannot be closed as usual), at midjoint of middle finger of left hand, and near internal malleoli of both ankles. He cannot rise on his toes as well as usual and does so with considerable pain. Is quite wretched and could not be kept on this diet any longer. There is possibly some fluid in midphalangeal joint of midfinger of left hand. Same point on right hand is slightly sensitive to pressure. "Jumps" visibly if a sore point is touched. Ate no supper last night or breakfast or dinner today. Candy to be stopped. Has had none since 4 P.M. yesterday.

February 20. Much better. Points still showing tenderness are wrists and hands, which are much improved. Took one meal of graham-cracker diet yesterday and all three today.

February 21. A trace of tenderness in one joint only.

February 22. Feels very well.

February 23. Diet changed to a mixed one of 1512 calories.

This patient's further progress was uneventful, and he went home feeling entirely well on March 23, except that on March 3, under some rather forced mixed feeding to make up for the loss of

weight sustained during this last attack, patient developed some toothache, a red throat, some joint discomfort, and fever, the latter up to  $100\frac{2}{3}^{\circ}$ . He had been losing weight or remaining stationary, but as the result of this feeding had gained five pounds in all. His diet was again sharply cut and he improved at once. The patient was still well six weeks after leaving the hospital, and though he deliberately departed from his diet after July, and gained 20 pounds, he was in very fair shape in November, 1915.

The results in this case seemed pretty clear. There could be no question of his original illness; of his marked convalescence; of the exacerbation under the sugar feeding; of his prompt convalescence when the sugar was removed (hastened, possibly, by his refusal of all food for nearly twenty-four hours), or of the excellence of his condition when he left the hospital. The only doubt that can enter is, whether there could have occurred a severe exacerbation coincident with the experiment, such as those noted early in the course of treatment and referred to above. The diminishing nature and frequency of these attacks, their practical cessation under strict diet and their somewhat different character make this unlikely.

CASE XXXVI.—Miss C., aged thirty-five years, referred by the courtesy of Dr. E. H. Goodman, came under observation February 1, 1915, and was discharged July 7, 1915. An arthritis of four years' intermittent duration involved the jaws, shoulders, elbows, hands, knees, and ankles. The patient had wide-spread and severe psoriasis, involving nearly every part of the body. Treatment of this case developed several points of interest. Her previous treatment had included vaccines and radium water. She began to improve on a house diet of 1718 calories. On February 18 she was given a diet of 75 gms. of graham crackers, 1 apple, 5 gms. butter, and 9 gms. sugar at each meal, yielding 1410 calories a day, with the idea of maintaining the joint improvement and at the same time helping the psoriasis along lines indicated by the interesting work of Schamberg, Ringer et al.<sup>4</sup>

These authors have shown that there is in psoriasis a strong tendency toward the retention of nitrogen and that a curtailment of the nitrogen intake to a minimum may be followed by great improvement or cure. By March 16, 1915, it was evident that the psoriasis had improved about 75 per cent., but that the joints, after having made substantial progress and changed their shape, were "hanging fire." She was then put upon a mixed diet of 1002 calories, on the possibility that the carbohydrate intake was too high. After eight days she had lost 9 pounds *in toto* from the start, her weight being 110 pounds. It was thought that a still more restricted diet was indicated, but that preparatory to putting

<sup>4</sup> Research Studies on Psoriasis, Schamberg, Kolmer, Ringer, and Raiziss, *Jour. Cutan. Dis.*, October and November, 1913.

her upon it an effort should be made to increase her weight and strength. This was a mistake, but she was put back, March 24, 1915, on a fuller diet, very high in carbohydrates but low in nitrogen, and consisting of bread, potatoes, rice, etc. The hope was that the psoriasis could be held in abeyance while her weight was increased even at the expense of her joints, but she relapsed so promptly and severely that on March 30, 1915, the psoriasis was everywhere violent and the arthritis as bad as it had ever been, or worse. It was felt that radical measures alone would do her any good, and she was put upon a graham-cracker diet as above of 846 calories. The joints responded at once, objectively as well as subjectively, and by April 11, 483 calories of fat had been added in the shape of olive oil and butter, with the idea of increasing her weight, which had gone down to 103 pounds, and also of testing out her tolerance for fat as compared with carbohydrate. Her weight reached 101 and then began to climb. The psoriasis showed no real improvement this time on the low nitrogen diet, though the nitrogen intake was lower than before, and at her request she was given, by Dr. F. C. Knowles, on April 13, an ointment containing liquor carbonis detergens and salicylic acid, after which the psoriasis improved. Her further progress was steady, and by April 21 she was taking 2054 calories, of which only 860 came from the graham crackers and apples. On June 14, 1915, the woman was practically well of both her psoriasis and joint disease, save for a very trifling sensitiveness on lateral pressure over the middle knuckle of the right midfinger. The ointment had been stopped on June 2. She had often previously been on full doses of the salicylates without benefit, and was two weeks convalescent as to her joints when the ointment was started.

It was thought that this would be a good case in which to try the effect of high carbohydrate feeding, as in the last 2 cases, so on June 20, all fat was substituted by pure carbohydrate in the form of peppermint candy. She was getting a total of 2053 calories, of which 1207 came from fat and whisky. This was substituted by 300 gms. sugar, equivalent to 1200 calories, but as no injury was apparent on the 24, she got a further addition of 40 gms. corn-starch and 35 gms. sugar, equivalent to 300 calories, making the total 2353. On June 26 she was still well, however, except for a bad headache, and could not force down her food, so the experiment was stopped. She was put back on the high fat diet, substituting saltines for graham crackers, and left for home July 6, apparently perfectly well. Before the forced carbohydrate feeding her weight had come up under the fat to 105, and when she left it was 109 pounds. It is hard to escape the view that the psoriasis was a complicating factor in this case. The caloric reduction was almost the lowest the writer had ever reached in treatment, and shows the freedom from danger, under properly

guarded conditions, of such extremities if they become necessary. No exacerbation of her disease was caused by the high carbohydrate feeding within the period covered. What might have happened had the diet been continued cannot be said, though it is noteworthy that the next case to be described behaved analogously for the same period of time, and then developed a sharp exacerbation while still under the forced feeding. It is possible that the strong tendency toward retention of nitrogen which psoriatics show was a factor which added to the difficulty of treatment. It should be added that joint cases which recover along these lines acquire in most instances an increased tolerance for food if they adhere carefully to their regime. This is beyond question, and is possibly an added reason for the tolerance shown in the experiment last recorded, since she had been upon a limited intake of carbohydrate for twelve weeks, and was almost perfectly well at the time. Properly to test the effect of carbohydrate her maximum intake when well should have been exceeded by a much greater margin, but this was hardly possible of accomplishment. On January 21, 1916, this patient was apparently in robust health, weighing 122 pounds, eating much more generously, and walking on some days as much as eight miles. It is interesting to note that throughout her illness at the hospital she had, and still has, a carious molar tooth, which cannot be ignored as a possible source of infection. Her recovery in spite of this is in keeping with other such instances already cited.

CASE XXXVII.—Fred M., aged thirty-nine years, referred by the courtesy of Dr. A. H. Gerhard, was admitted April 24, 1915, and discharged July 9, 1915. An arthritis of fourteen months' duration involved the shoulders, elbows, wrists, hands, knees, and feet, and incapacitated him. A probationary house diet yielded 2078 calories. He was given a mixed diet of 1268 calories, on which he showed slight improvement. This was changed on May 15, 1915, to 1065. He developed tonsillitis on May 25, after showing evident improvement, and was held back somewhat. By June 15 he was in very good shape, and a feeding experiment with carbohydrate was begun. He was put on a diet of graham crackers 60 gms., apple 150 gms., and weak tea with 7 gms. sugar, three times a day, yielding 1072 calories. On June 20 he got 322 gms. of candy, equivalent to 300 gms. of cane-sugar, distributed during the day. This added 1200 calories, making a total of 2272. On June 24, 40 gms. of cornstarch and 35 gms. of cane-sugar were added to the intake daily, cooked with water and a little vanilla, and making a bulk of 546 gms. This yielded in all 2572 calories. The notes follow:

June 26. For the first time since the forced carbohydrate feeding he seems to have more pain, chiefly in both wrists. Left knee slightly stiffer.

June 27. Says he felt worse when he woke up today than for some time past. At 5 p.m. has increased pain in both wrists, left little finger, left thumb, left ankle, shaft of left arm, and left knee.

June 28. Worse. Points of soreness are right side of chest posteriorly, right side of neck, right knee, left shoulder, both wrists (worse than yesterday), left forefinger, left little finger, left knee, and both ankles.

June 29. Worse. Additional points are the right shoulder, toes, and left pectoral muscles. Diet cannot be pushed further. To return to simple graham-cracker diet tomorrow.

July 1. Has made undoubted progress and is better considerably today at eleven points.

July 3. Right and left little fingers and both wrists are somewhat worse. Right knee shows effusion. Other points are better or well.

July 5. Effusion less. Distinctly better elsewhere.

July 8. Progress satisfactory but not yet back to his condition before the experiment. He grew very tired of the diet and was returned, on July 7, to a mixed diet of 1072 calories. Sent home with instructions to follow the diet for the rest of the summer and report in the fall.

In this case there could be no doubt of the exacerbation induced by the forced feeding. The man was made almost worse than he had been at any time. Also, he had had no prior exacerbations of a nature to be confusing. It is interesting to note, as mentioned in the last case, that these two cases happened to be carried through on exactly the same dates, and that the present case had hardly begun to have symptoms—had certainly shown none that were definite—by the date upon which the former had to be taken off her forced diet without having shown an exacerbation.

Reference is omitted to several other cases under treatment at the present writing.

OBSERVATIONS ON THE HYDROGEN ION CONCENTRATION OF THE URINE AND THE CARBON DIOXIDE TENSION IN THE ALVEOLAR AIR. As already referred to in the text, observations have been conducted in some cases of this series on the hydrogen ion concentration of the urine, as a measure of the true urinary acidity. The methods followed were those developed by Henderson and Palmer,<sup>5</sup> and depend upon the comparison of diluted urine, to which an indicator has been added, with a series of flasks of prepared solutions. These solutions contain weighed amounts of the sodium and potassium salts of phosphoric and acetic acids, and correspond to definite concentrations of the hydrogen and hydroxyl ions, which, in terms of physical chemistry, express acidity and alkalinity. The notation used signifies the logarithm of that number which

<sup>5</sup> Clinical Studies on Acid Base Equilibrium and the Nature of Acidosis. Walter W. Palmer, Lawrence J. Henderson, Archives Int. Med., August, 1913, xii, 153-170.

expresses the actual acidity or alkalinity. The logarithm decreases as the acidity increases, and *vice versa*, and the minus sign is here omitted.<sup>6</sup>

A study of the figures shows that until the patients were placed upon the standard graham-cracker diet no characteristic reactions could be discerned, although the urines in disease and convalescence were contrasted. Cases in apparently comparable stages of the disease gave varying results, and the same case at the same period sometimes showed variations from marked acidity to marked alkalinity.

The samples were from twenty-four-hour specimens, preserved with toluol and kept on the ice. Doubtful ones were discarded. Occasionally, "stat" specimens were also examined. Space will not permit of giving the figures for the cases which were not placed upon the standard graham-cracker diet.

The first case examined upon the standard diet was in Case XXXV. The urine showed the same indefinite variation on the probationary house diet, and when the patient was convalescent on it, but when he was convalescent on a constant mixed diet it approximated stability of reaction. Around January 10, it showed an interesting drop from an acidity of 6 or thereabouts to one of 7.7, a difference of 4.5 in the scale of eleven flasks, from which it slowly recovered. Coincident with this was an exacerbation of his arthritic condition, the urinary change slightly anticipating the attack. This was repeated sufficiently often in this and other cases to suggest that it is a feature of such disturbances, and reflects a metabolic change whose nature is not yet clear. In two instances it led to the anticipation of otherwise unsuspected oncoming attacks, but sometimes appeared immediately afterward. These changes can be seen by consulting the appended tables, and occurred as follows: Case XXXV, as recorded above and again accompanying an exacerbation on January 24. Again on February 19, accompanying an attack produced by carbohydrate feeding. Case XXXIV, on January 11, accompanying an ephemeral exacerbation in one hip and about January 26, accompanying an exacerbation induced by carbohydrate feeding. There was one isolated drop in the acidity on January 6, which was accompanied by no noteworthy symptoms and cannot be explained. It may have been due to an error in the collection.

Case XXXVI showed a less constant reaction during the period observed on the basal cracker diet, owing probably to the error of feeding asparagus which necessarily varied in quality, water

<sup>6</sup> It should be here stated that the logarithmic figures do not portray graphically the differences in reaction of the urine, as a drop from No. 7 to No. 4 in the scale of eleven flasks, three members of the series, is indicated merely by the change from 6 to 7 in the logarithm. This should be borne in mind by those unfamiliar with the notation.

content, etc., and it is interesting to note that the high carbohydrate feeding *per se* made no great change in the hydrogen ion concentration during the period observed. This is in keeping with the observations of Blatherwick on the effect of the ash in diets, and additionally suggests that the change in the cases of induced exacerbation depended upon the systemic disturbance. Owing to the failure to induce an exacerbation the figures are omitted to save space.

Case XXXVII showed the same reduction beginning around January 25, coincident with an attack induced by forced carbohydrate feeding. In the cases above mentioned, the reaction of the urine did not always return at once to its original level but remained alkaline or less acid for some time. The reaction of the urine depends chiefly upon the relative amounts of the dimetal hydrogen phosphate and the monometal dihydrogen phosphate present. A decrease in the acidity as here found represents in the urine an increase of the dimetal (disodium or potassium) hydrogen phosphate as compared with the monometal (monosodium or potassium) dihydrogen phosphate. The metabolic cause of this urinary change remains a subject for future investigation.<sup>7</sup> The long period required to bring these patients into the convalescent or recovered condition, together with the further period and coöperative difficulties incidental to the induction of a clear exacerbation, seem to warrant the presentation of these cases now.

The urinary findings need corroboration from a longer series before they can be accepted as established and observations are pending to that end.

CASE XXXV.—James N. November 17, 1914. Log. = 6.7. Convalescing on house diet averaging 2170 calories.

November 17. Log. = 5.7. "Stat" specimen. Noon: house diet.

November 18. Log. = 6.3. House diet.

November 18. Log. = 7.4. "Stat" specimen. Noon: house diet.

January 5, 1915. Log. = 5.7. 1663 calories of mixed diet; three days convalescent from a "flare up" in the course of recovery.

January 6. Log. = 5.3. 1663 calories of mixed diet. Very well.

January 7. Log. = 5.7. 16S3 calories of graham crackers and milk. Well.

January 8. Log. = 6. 3650 c.c. ditto.

January 9. Log. = 6. 2485 c.c.

January 10. Log. = 6.3. 2100 c.c.

January 11. Log. = 7. 1530 c.c.

January 12. Log. = 6.7. 1120 c.c. Exacerbation on night of January 11, on Blatherwick's diet.

<sup>7</sup> Since the completion of the above work, Wilson, Stearns and Janney have reported an alkalosis after parathyroideectomy in dogs. *Journal of Biological Chemistry*, November, 1915.

January 13. Log. = 7.7. 910 c.c. Still sick and effusion in knee.

NOTE.—To test the effect of varying the volume as a possible contributory cause of this difference, the urines of Cases XXXV and XXXIV were diluted in varying amounts up to 100 and 300 per cent. greater volume respectively, but gave the same figures. Except where specified, the specimens were taken from twenty-four-hour collections.

January 14. Log. = 6.3. 1980 c.c.

January 15. Log. = 5.85. 1800 c.c. Well.

January 16. Log. = 5.85. 1840 c.c. 2649 calories started yesterday.

January 17. Log. = 6.3. 2190 c.c. 1827 calories started yesterday at lunch. Now on low proteid diet of graham crackers.

January 18. Log. = 6.2. 1080 c.c.

January 19. Log. = 5.85. 1960 c.c.

January 20. Log. = 6. 2390 c.c.

January 21. Log. = 6. 1870 c.c.

January 22. Log. = 5.85. 1110 c.c.

January 23. Log. = 6.85. 1780 c.c. Well.

January 24. Log. = 6.5. 2160 c.c. Exacerbation last night.

January 25. Log. = 7. 1790 c.c. Effusion in knee still left.

January 26. Log. = 7. 2000 c.c. Well; some effusion still left.

January 27. Log. = 7. 1930 c.c. Well.

January 28. Log. = 7. 2300 c.c.

February 14. Log. = 6.3. 1810 c.c. Graham-cracker diet 1827 calories. Very slight attack in one joint. Began 6 A.M. Gone by noon, almost.

February 15. Log. = 6. 1530 c.c.

February 16. Log. = 6.15. 1810 c.c.

February 17. Log. = 6.7. First urine after candy feeding. 1820 c.c.

February 18. Log. = 6.3. Below par.

February 19. Log. = 7. 1100 c.c. Sharp attack. No effusion.

February 20. Log. = 6.85. 700 c.c. No breakfast or dinner yesterday. Candy stopped yesterday.

February 21. Log. = 5.85. 660 c.c. Practically well.

February 22. Log. = 5.85. 1600 c.c. Well.

February 23. Log. = 6. 1620 c.c.

March 6. Log. = 5.7. 2420 c.c. Mixed diet of 1512 calories started February 23.

March 7. Log. = 5.7. 1880 c.c.

March 8. Log. = 5.6. 1360 c.c. Fever today; joints worse; patient caught "cold."

March 9. Log. = 5.85. 1730 c.c.

March 10. Log. = 5.5. 1590 c.c.

CASE XXXIV.—(Mrs. S.)—November 17, 1914. Log. = 5.7. House diet averaging 1892 calories.

November 17. Log. = 5.7. "Stat" specimen at noon.

November 18. Log. = 6.

November 18. Log. = 5.2. "Stat" specimen.

January 5, 1915. Log. = 5.7. Well.

January 6. Log. = 7.

January 8. Log. = 5.85. 410 c.c.

January 9. Log. 6.5. 800 c.c. Comparison not good. Exacerbation in hip.

January 10. Log. = 5.85. 700 c.c. Diet of 1089 calories of graham crackers and three glasses of milk begun today at breakfast.

January 11. Log. 7.7. 1000 c.c. Exacerbation in hip better.

January 12. Log. = 5.3. 380 c.c. Well.

January 13. Log. = 5.85. 330 c.c.

January 14. Log. = 5.5. 460 c.c.

January 15. Log. = 5.5. 300 c.c. Well.

January 16. Log. = 5.5. 420 c.c.

January 17. Log. 5.5. 410 c.c.

January 18. Log. = 5.5. 520 c.c.

January 19. Log. = 5.5. 410 c.c. Candy started with 66 gms. of cane-sugar b. d. 528 calories per diem; total calories 1617.

January 20. Log. = 5.7. 610 c.c. Menstruating.

January 21. Log. = 5.85. 630 c.c.

January 22. Log. = 5.5. 280 c.c. Costive.

January 23. Log. = 5.7. 530 c.c.

January 24. Log. = 5.7. 315 c.c.

January 25. Log. = 6. 530 c.c.

January 26. Log. = 5.85. 350 c.c. Induced exacerbation.

January 27. Log missing. 510 c.c. Candy stopped on January 26.

January 28. Log. = 6.7. 660 c.c. Better, but distinctly sore. Effusion in elbow bursa.

January 29. Log. = 5.85. 550 c.c.

CASE XXXVII (Fred M.).—June 16, 1915. Log. = 5.5. 500 c.c. On graham-cracker diet of 1072 calories. Urine scanty and full of urates.

June 17. Log. = 5.5. 810 c.c.

June 18. Log. = 5.7. 460 c.c.

June 19. Log. = 5.6.

June 20. Log. = 5.5. 300 c.c.

June 21. Log. = 5.5. 310 c.c.

Beginning yesterday got 300 gms. of cane-sugar daily, 1200 calories, or 2272 calories in all.

June 22. Log. = 5.6. 360 c.c. Not quite so well.

June 23. Log. = 5.8.

June 24. Got additional 300 calories from cornstarch and cane-sugar.

June 25. Log. = 5.8. 350 c.c.

June 27. Log. = 5.85. 280 c.c.  
 June 28. Log. = 6.3. 450 c.c. Exacerbation.  
 June 29. Log. = 6.2. 570 c.c.  
 July 1. Log. = 6.4. 340 c.c. Somewhat better.  
 July 2. Log. = 6.4. 340 c.c.  
 July 3. Log. = 6.4. 320 c.c. Worse.  
 July 4. Log. = 6.2. 320 c.c. Slightly better.  
 July 5. Log. = 6.3. 320 c.c.  
 July 6. Log. = 6.2. 315 c.c. Doing well.

In view of the urinary changes recorded above, and with a view to throwing light on a possible acidosis as well as for other reasons, observations were conducted on the carbon dioxide tension of the alveolar air in several of these cases during ill health and convalescence.

Higgins's<sup>8</sup> adaptation of the Plesch method was employed, using 1000 c.c., as suggested by Boothby and Peabody.<sup>9</sup>

The analyses were made with a Tutweiler mercury gas burette as modified and used by the United Gas Improvement Company of Philadelphia.<sup>10</sup>

Comparisons were first made of the results obtained by using 1000 c.c. of air, and by the exhalation method, the former being finally selected as less variable, though the difference was not great, as pointed out by the above authors.

As seen by the accompanying tables the normal cases undoubtedly averaged slightly higher than the arthritis cases, but while this is suggestive, the difference is not greater than may possibly be accounted for by the fuller diets of the normal cases. Further observations are pending on this point. It is interesting to note, however, that T. K., with active arthritis and on a house diet, had low figures. Fred. M., Case XXXVII, while convalescing on 1072 calories of a graham-cracker diet, averaged less than 32.06 mm., and during an induced exacerbation getting 2572 calories daily of nearly pure carbohydrate, gave an average of only 40.5 mm.

Case XXXVI, Miss C., gave low figures throughout, although at the time getting 2054 calories, supplied chiefly by graham crackers, fat, and whisky. When getting nearly 1000 calories more than Case XXXVII she gave even lower figures than he did. It is evident, therefore, that the conclusion to be drawn at the present writing is that there is no great change of the alveolar carbon dioxide tension characteristic of rheumatoid arthritis. There may be one of minor degree, but further observations are necessary to establish this point.

<sup>8</sup> The Influence of Food, Posture and Other Factors on the Carbon Dioxide Tension in Man, *Am. Jour. Physiol.*, April 1, 1914, xxxiv, No. 1.

<sup>9</sup> A Comparison of Methods of Obtaining Alveolar Air, *Archives Int. Med.*, March, 1914, xiii, 497-506.

<sup>10</sup> The writer wishes to express his marked appreciation to Mr. George H. Fulweiler, chief chemist of the United Gas Improvement Company, for courtesy and assistance in this connection.

OBSERVATIONS ON THE CARBON DIOXIDE TENSION OF THE  
ALVEOLAR AIR.

NORMAL CASES.

R. P.:

|               |       |         |            |                             |
|---------------|-------|---------|------------|-----------------------------|
| May 14, 1915. | 41.60 | mm. Hg. | 12.30 p.m. | Four hours after breakfast. |
| May 17, 1915. | 41.20 | "       |            |                             |
| May 18, 1915. | 39.41 | "       | 3.15 p.m.  |                             |
| May 18, 1915. | 41.20 | "       | 4.30 p.m.  |                             |
| June 2, 1915. | 39.63 | "       | 7.00 p.m.  | Lunch at 2 p.m.             |
| June 3, 1915. | 42.17 | "       | 10.30 a.m. | Breakfast at 8.30 a.m.      |

Michael:

|               |       |   |           |                      |
|---------------|-------|---|-----------|----------------------|
| June 9, 1915. | 43.08 | " | 5.00 p.m. | Dinner at 11.30 a.m. |
|               | 45.35 | " |           |                      |

J. F.:

|                |       |   |           |                |
|----------------|-------|---|-----------|----------------|
| June 15, 1915. | 39.66 | " | 6.10 p.m. | Lunch at noon. |
|----------------|-------|---|-----------|----------------|

Dr. L.:

|                |       |   |           |                      |
|----------------|-------|---|-----------|----------------------|
| June 16, 1915. | 39.1  | " | 6.00 p.m. | No food since 1 p.m. |
| June 16, 1915. | 41.00 | " | 6.25 p.m. | No food since 1 p.m. |

ARTHRITIC CASES.

T. K.—In active arthritis and on house diet:

|               |       |         |            |                 |
|---------------|-------|---------|------------|-----------------|
| June 2, 1915. | 34.21 | mm. Hg. | 5.30 p.m.  | Dinner at noon. |
| June 3, 1915. | 32.94 | "       | 11.00 a.m. | No breakfast.   |

Took 200 gms. cane-sugar and juice of one and a half lemon in water at noon.

|               |         |            |            |                  |
|---------------|---------|------------|------------|------------------|
| 35.03         | mm. Hg. | 12.15 p.m. |            |                  |
| 36.92         | "       | 12.40 p.m. |            |                  |
| 35.13         | "       | 1.05 p.m.  |            |                  |
| 36.37         | "       | 1.30 p.m.  |            |                  |
| 36.01         | "       | 1.50 p.m.  |            |                  |
| 36.88         | "       | 2.35 p.m.  |            |                  |
| 38.02         | "       | 3.20 p.m.  |            |                  |
| 37.36         | "       | 3.50 p.m.  |            |                  |
| 38.45         | "       | 4.20 p.m.  |            |                  |
| June 4, 1915. | 37.63   | "          | 4.50 p.m.  | Dinner at 12.30. |
| June 5, 1915. | 36.62   | "          | 10.55 a.m. | No breakfast.    |

CASE XXXVI.—Miss C. Doing well. Getting 2054 calories of graham crackers and fat.

|                |       |         |           |                          |
|----------------|-------|---------|-----------|--------------------------|
| June 11, 1915. | 30.44 | mm. Hg. | 4.00 p.m. | No food since 12.15 p.m. |
|                | 32.86 | "       | 5.00 p.m. |                          |
|                | 29.05 | "       | 5.40 p.m. |                          |
| June 15, 1915. | 30.39 | "       | 4.30 p.m. | Lunch at 12.30 p.m.      |
|                | 28.72 | "       | 5.00 p.m. |                          |
| June 19, 1915. | 33.10 | "       | 9.40 a.m. | No breakfast.            |

Average of two experiments.

CASE XXXVII.—F. M. Pretty well on 1672 calories of graham crackers, etc. Some traces of trouble left yet.

|                |       |         |            |   |
|----------------|-------|---------|------------|---|
| June 17, 1915. | 29.39 | mm. Hg. | 4.50 p.m.  | Lunch at 12.30 p.m.   |
|                | 34.74 | "       | 5.15 p.m.  | Breathing too slowly and result too high.                                     |
|                | 32.05 | "       | 5.40 p.m.  |   |
| June 19, 1915. | 35.35 | "       | 11.00 a.m. | Before breakfast.   |
| June 28, 1915. | 41.17 | "       | 4.00 p.m.  | No food since lunch, but is on the forced carbohydrate diet of 2572 calories. |

Distinctly worse:

|       |   |           |
|-------|---|-----------|
| 35.95 | " | 4.40 p.m. |
| 40.38 | " | 5.05 p.m. |

In the studies previously reported were included observations on the urea and non-coagulable nitrogen of the blood in rheumatoid arthritis which gave entirely normal values. In view of the opportunity, however, to make comparisons in this respect between health and disease, observations were begun to that end, but only one was completed in time to be published. Blood was therefore analyzed from other cases, first before treatment and then when they were convalescent or had recovered under treatment.

The first 3 were ill and no opportunity was afforded to get the blood a second time as they left the hospital, but the figures are given as showing further the normal values. The conditions were as previously reported. It is seen that there is no appreciable difference in the blood findings during active arthritis and those taken during the convalescent or recovered period. The analyses were made by Dr. Charles W. Lüders, to whom acknowledgment is due. Since the completion of this work, Folin and Dennis have reported<sup>11</sup> analyses of uric acid and non-protein nitrogen in 5 cases of arthritis deformans among a larger series of gouty and other patients. These writers conclude that: (1) "In gout the blood is almost invariably abnormally high in uric acid, while the other waste products represented in the non-protein nitrogen of the blood are usually within the normal limits. In arthritis also the blood is not infrequently abnormally high in uric acid but most such cases have abnormally high non-protein nitrogen as well. (2) Neither qualitative tests for uric acid in the blood nor quantitative determinations of the uric acid alone can be depended on in the differential diagnosis of gout and other joint diseases. (3) For a differential diagnosis in doubtful cases of gout or arthritis by means of blood analyses the patient must be on a purin-free diet and uric acid determinations must be accompanied by determinations of the non-protein nitrogen (or urea)."

In their series only 1 of the 5 cases of arthritis deformans gave very high values for non-protein nitrogen (104 mgs.) the others being in the neighborhood of 60 mgs. per 100 c.c. blood, but as the figures of these careful workers are at variance with those of the present writer and imply a means of differentiating doubtful cases of rheumatoid arthritis from doubtful cases of gout, it seems well to include here, with the new cases, those already reported, since they illustrate the great uniformity and low values of the findings in a total of 9 cases of rheumatoid arthritis. These 9 instances were in relatively young individuals free from complicating diseases. They all represented clear-cut examples of rheumatoid arthritis and on 3 of them the analyses of ill health were repeated during recovery with practically identical results. These observations were conducted by two sets of observers, and there seems hardly

room for the possibility of error in the technic. The simplest explanation of this discrepancy is that the cases studied by Folin and Dennis may have had some complicating factor.

| Old series.                                    | Total non-coagulable<br>nitrogen in mg. per<br>100 c.c. blood. |      |       | Urea in mg. per<br>100 c.c. blood. |      |      |
|--|--|------|-------|------------------------------------|------|------|
|  | Average.   |      |       | Average.                           |      |      |
| Case VIII. Patient ill                         | 20.2   | 21.7 | 21.00 | 11.2                               | 12.6 | 11.9 |
| Case IX. Experiment 1.<br>Patient ill          | 27.8   | 25.7 | 26.00 | 14.7                               | 14.5 | 14.6 |
| Case XI. Patient ill                           | 22.6   | 22.7 | 22.65 | 9.3                                | 10.2 | 9.6  |
| Case IX. Experiment 2.<br>Patient convalescent | 27.0   | 26.4 | 26.70 | 12.8                               | ..   | 12.8 |
| Case XIII. Patient ill                         | 24.6   | 25.5 | 25.00 | 12.0                               | 14.2 | 13.1 |
| Case XII. Patient ill                          | 24.4   | 25.0 | 24.70 | 10.4                               | ..   | 10.4 |

  

| New series.                        | Total non-coagulable<br>nitrogen in mg. per<br>100 c.c. blood. |  |  | Total urea in mg.<br>per 100 c.c. blood. |       |  |
|------------------------------------|--|--|--|--|-------|--|
|                                    | Average.   |  |  | Average.                                 |       |  |
| Mrs. B. Ill                        | 21.60  |  |  | ..                                       | 16.10 |  |
| Mrs. S. (Case XXVI). Well          | 32.30  |  |  |  |       |  |
| Mrs. C. (Case XXVII).<br>Improving | 26.30  |  |  |  |       |  |
| Mrs. S. (Case XXXIV). Ill          | 28.70  |  |  | Ill                                      | 12.37 |  |
| Mrs. S. (Case XXXIV).<br>Well      | 26.20  |  |  | Well                                     | 14.70 |  |
| James N. (Case XXXV). Ill          | 26.07  |  |  | Ill                                      | 12.35 |  |
| James N. (Case XXXV).<br>Well      | 28.30  |  |  | Well                                     | 15.70 |  |

**DISCUSSION.** A review of the foregoing permits of certain general conclusions. In the first place it is plain from the end-results of Series 1 that cases of rheumatoid arthritis treated along the lines of dietary curtailment, as indicated, will, by and large, indefinitely retain the improvement which may have occurred, provided they adhere to the general principles already followed. A number of cases have now been followed for a long time after recovery, the longest period being nearly five years.

In the second place, it is plain from an extension of the method to another and longer series that a large proportion of cases will show a response to treatment, there being 1 instance (Case XXX) in the 37 here recorded where no influence could be observed. In a definite proportion of cases so responding, treatment may be limited by intercurrent conditions and the desired end-result may be modified or entirely prevented. It was prevented in 1 of the cases which responded and remained under observation (Case XXI).

There are also limitations in cases emaciated or bed-ridden, where a curtailment of diet is in itself contra-indicated. Such cases must be improved in nutrition before they can be successfully carried through. In other words, there is nothing in these dietetic measures *per se* which is harmful if carefully watched, but there are advanced cases of rheumatoid arthritis which have gotten to the point where

any serious disturbance of their routine is dangerous to their already precarious health.

In these cases the arthritis can generally be influenced, but perhaps only at the expense of their already broken health. The writer desires to emphasize this. Even in such extreme types, however, something may be accomplished, and the effort is often well worth while if these truths be appreciated. It is also possible that subsequent study may show more types of cases which do not respond at all to these measures, as already illustrated by Case XXX, and the present report aims to present nothing more than the statistics to date. On the other hand, there can now be no doubt of the entire success of these measures in a great number, perhaps the great majority of sufferers from this disease if they be taken in hand early.

The writer wishes to emphasize again that there is nothing here which controverts the general view that many cases are precipitated or perpetuated by foci of infection. If these foci can be removed, such a step is the easiest and quickest way out for the patient. Unfortunately this is not always possible and frequently failure attends repeated effort to that end. However that may be, the most interesting point in this connection is that *cases showing unmistakable and obvious sources of possible infection in teeth, tonsils, or elsewhere, may improve or recover completely upon a dietary régime.* This is now unquestionable. The real explanation is not at hand.

Too much emphasis cannot be laid on the precautions to which attention has elsewhere been called.<sup>12</sup> Furthermore only minute attention to detail will achieve results and repeated changes in the dietaries may be required.

The writer has suggested previously upon several counts that the large bowel is not chiefly or directly responsible for the symptoms, as has been maintained by some writers, and the experience with Case VII bears this out.

As has been elsewhere noted, several cases of the last series showed some beginning improvement upon the regular house diet. The reason is obvious. If the food tolerance of patients happens to be high, as is often the case, the limited intake of the house diet may be helpful. For example, the evening meal at the Presbyterian Hospital in Philadelphia yields on the average only some 400 calories, and consists of a slice or two of bread, a cup of tea or milk, and some stewed fruit. This house diet, however, is rarely sufficient to maintain improvement, as it is too uncertain; and after obtaining an idea therefrom, in these instances, the total calories have been put safely below that level and made to come from con-

<sup>12</sup> The Nature and Successful Treatment of Rheumatoid Arthritis, Internat. Clin., iii, Series 24.

stant sources. In Cases XXXV and XXXVI the improvement which had begun on the house diet was not maintained and changes of diet were necessary. In the limited space at disposal no reference can be made to all the dietary changes in the various cases. The use of calories as a measure of the amount of food is of course for that purpose only and is not meant to imply necessarily any change in the caloric needs of the body.

The after-treatment of these cases is often important. After the arthritis has subsided the weight may be much lowered, and at about that period the writer has been in the habit sometimes of giving cod-liver oil. It is important to maintain the food level fairly constant for some time and to make additions very slowly, watching the result of each one. Orthopedic exercises are generally indicated, but cannot, of course, be undertaken until the patient has become well accustomed to the new level of equilibrium or has begun to gain weight. The question of the low caloric level at which some of these cases have improved, and indeed continued to live, is a large problem in itself, and brief reference only can be made to it. When the writer first published his results, these diets seemed somewhat iconoclastic, but the experiences of Dr. F. M. Allen in the low feeding of diabetics has since shown how eminently safely this can be carried to even a much further point. There is reason to suspect that some cases of rheumatoid arthritis have a lowered necessity for food as compared with most individuals, or at least with the necessity standards as now accepted. Reference has elsewhere been made to the suggestive overlapping of the symptoms of acute inflammatory rheumatism and those in some cases of chronic arthritis. Illustration of this is to be seen in Cases XXIII and XXIV, as well as in some of the exacerbations of Cases XXXIV and XXXV. It is, of course, not to be understood that acute inflammatory rheumatism and rheumatoid arthritis are regarded as identical, but some symptoms of the former may occur in the latter condition, strongly resembling the redness, swelling, pain, and fever of the acute variety. The undoubtedly improvement shown under dietary measures strongly suggests a common factor in some of these instances.

No drugs were given in the present series except where stimulation was needed, and, on one or two occasions, where treatment was interrupted. It should be stated that the writer has seen a considerable number of other cases to which no reference is made (many of them referred by his colleagues) because they have not been suitable for treatment or have improved upon the removal of the infectious foci, which step has nearly always been advocated where possible. One case, referred by the courtesy of Dr. Wm. G. Spiller, presented a long-standing ankylosis of both hips. It could not be determined that any active process was present or that any specific benefit followed upon treatment, although the

patient chose to keep to his diet, and writes that he feels in better general health.

Case XXXIV was of the type in which the large joints chiefly were involved, and it is interesting to note, as in some others, that the same favorable results were obtained. Multiple fibrous nodules, easily mistaken at times for bony formations, were present in Cases XXVIII and XXIX, and showed striking resolution under treatment.

In chronic cases long upon a fixed diet, attacks of slight nausea, diarrhea and the like may occur, requiring mild catharsis and temporary suspension of the diet. Such attacks are apt to be accompanied by exacerbations. Also, it sometimes happens that long-standing cases who may do well for as much as six weeks, require further curtailment of diet even after marked improvement has occurred.

It has seemed important to emphasize with the second series a few of the points already mentioned in order to define the limitations and possibilities in these measures. Many minor points have been omitted, but it is hoped that the general principles have been made clear enough to enable others to obtain results. The sequelæ of long-standing rheumatoid arthritis are such that they, rather than the actual arthritis, often present the greatest obstacles. It is to be remembered that the arrest of the causative arthritis does not undo the harm done or transform a cripple, and that even after the causative disease is no longer active there are many factors which may be productive of pains and disability. There is no short cut in the treatment of these patients and the lesson to be learned is to begin early in the disease, before deformity has occurred, at which period most gratifying successes may follow. It is also true that some long-standing cases respond surprisingly well and in such the causative arthritis may be arrested.

The results of the feeding experiments, in which out of four attempts upon patients rendered convalescent or well, exacerbations were induced in three by the ingestion of pure carbohydrate, seem pretty definite. The mechanism of this is not yet clear. It may prove referable to a bacteriological or other cleavage in the small intestine, but whether the process begins there and then or later, the end-effects are of a metabolic nature. Observations upon muscular exercise, not mentioned here, support this and also indicate pretty strongly that within certain limits and under certain conditions, a greatly increased food intake may be made possible by marked bodily activity, when this is permissible.

The one unsuccessful experiment with forced carbohydrate feeding above mentioned can be at least partly accounted for, as suggested under Case XXXVI. The human factor and the limited degree to which biological experiments can be pushed under these circumstances introduce great difficulties, and it is conceivable

that had it been possible to ignore them, the same results would have followed here as in the other three instances.

The principle which this article endeavors to point out is that rheumatoid arthritis is often referable to the dietary factors above indicated. The operation of this principle can be appreciated in a large majority of cases where the measures in question are applied and subsidence of the inflammatory process follows to a greater or less degree. This is independent of the question of complete restoration to health which is conditioned by various factors in which chronicity of the disease and its sequelae play an important rôle. As a matter of fact, however, a gratifying proportion of cases can be materially helped, as the above records show, and, in many, arrest of the disease process may take place.

The writer would like to express his obligation in a number of directions: To Dr. Alonzo E. Taylor, for helpful criticism and the use of his laboratories; to Dr. W. S. Newcomer, director of the Roentgen-ray department, for a long series of skilful co-operative studies; to Dr. Damon B. Pfeiffer, director of the pathological laboratory, for his helpful attitude at all times, and to the writer's colleagues on the staff of the hospital, for the use of beds in their wards, and other kindnesses.

Much obligation is also due to Miss Caroline Milne, directress of nurses; Miss Helen Wallace, chief dietician, and the nursing staff at the Presbyterian Hospital, on the last of whom has fallen the laborious work of preparing the weighed diets.

**CONCLUSIONS.** 1. The general conclusions already published as to the application of a restricted dietary in rheumatoid arthritis find confirmation within the limits indicated in the present series of 19 cases.

2. In cases rendered free, or nearly so, of acute symptoms by dietary means, exacerbations have been caused as an "experimentum crucis," by the ingestion of pure carbohydrate. Upon the withdrawal of this the symptoms have again subsided. The conclusion seems unavoidable that carbohydrate is a factor in the etiology and treatment of many cases of this disease.

3. Contemporaneously with natural or induced exacerbations of the disease there seems to be a tendency for the urine to show a decreased acidity, as measured by the hydrogen ion concentration.

4. Observations on the carbon dioxide tension of the alveolar air in these cases show no great departure from the normal.

5. The non-protein nitrogen and urea of the circulating blood in uncomplicated cases of rheumatoid arthritis, examined both during ill health and convalescence, fall well within the normal range.